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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/631,896	08/01/2003	Klaus Preissner	06478.1491	9809

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EXAMINER	
BOWMAN, AMY HUDSON	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 04/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/631,896	PREISSNER ET AL.	
	Examiner	Art Unit	
	Amy H. Bowman	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 February 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-12* is/are pending in the application.

4a) Of the above claim(s) *4-12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 3* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *8/1/2003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application/Amendment/Claims

Applicant's response filed 2/1/2006 has been considered. Rejections and/or objections not reiterated from the previous office action mailed 11/7/2005 are hereby withdrawn. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

This application contains subject matter drawn to an invention nonelected with traverse. Specifically, the subject matter drawn to RNA analogs, ribozymes, and aptamers in claim 1 is drawn to a nonelected invention. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Response to Arguments--Claim Rejections - 35 USC § 112

Claims 1 and 3 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for promotion of coagulation *in vitro* using RNA as a procoagulant cofactor, does not reasonably provide enablement for the treatment of a disease or disorder associated with coagulation via the administration of a pharmaceutical composition *in vivo*, as explained in the office action mailed 11/7/2005. Applicant has cancelled claim 2, obviating the rejection against this claim.

The instant rejection is based on the following premises. Firstly, the language "pharmaceutical preparation" in the preamble of claims 1 and 3 implies a therapeutic or treatment benefit that is not enabled because the instant specification, nor the art, has shown a pharmaceutical benefit. Secondly, the specification is not enabled because the instant specification, nor the art, has not taught how a PNA would enhance coagulation, as instantly recited.

Applicant asserts that the assays described in the specification reasonably correlate to the claimed method, i.e. promoting coagulation. Applicant asserts that the instant invention is not directed to delivery of the PNA, natural, or synthetic RNA into the cell to inhibit gene expression, as the office asserts. Art referring to the inhibitory affect of PNAs or the unpredictability of delivery of PNAs was only cited because the language "pharmaceutical preparation" in the preamble of claims 1 and 3 implies a therapeutic or treatment benefit that is not enabled and that would require delivery of the PNA. This art was also cited to exemplify the known inhibitory action of PNAs in the field since the instant specification does not teach how a PNA could promote coagulation as instantly claimed. Applicant points to sections of the specification that teach that extracellular RNA represents an important initial cofactor for the induction of coagulation.

Contrary to applicant's assertions, the specification does not reasonably provide enablement for the treatment of a disease or disorder associated with coagulation via the administration of a pharmaceutical composition *in vivo*. As explained in the office action mailed 11/7/2005, the language "pharmaceutical preparation" in claims 1 and 3 implies a therapeutic or treatment benefit that is not enabled. The *in vivo* promotion of

coagulation and resultant treatment effect described in the specification involves prophetic examples only and has not been reduced to practice.

There is no guidance in the specification as filed, either prophetic or by way of exemplification, that teaches how to administer the claimed pharmaceutical composition to cells or tissues *in vivo* and result in increased coagulation and a therapeutic or treatment effect. Applicant's arguments do not address this deficiency of the specification.

Additionally, the instant specification has not taught how a peptide-nucleic acid promotes coagulation. The specification teaches that extracellular RNA represents an important initial cofactor for induction of the coagulation cascade. The specification further teaches that pharmaceutical preparations have been developed in which natural or synthetic RNA or bioactive fragments of the RNA are added to promote hemostasis, however the specification also teaches that RNA-degrading and inhibiting compounds can inactivate the cofactor RNA, resulting in the RNA no longer being available for activation of FSAP or the contact system. The specification teaches that RNA-degrading or masking compounds can thus display important therapeutic effects which prevent initiation of the coagulation system and thus have pronounced anticoagulant effect. Since peptide-nucleic acids are known to target and inhibit RNA with increased specificity, the specification has not taught how one could predictably promote coagulation by administering a pharmaceutical composition comprising a peptide-nucleic acid. The only guidance given in the specification regarding such a mechanism is a statement that "ribonucleases might also display an anticoagulant effect on

ribozymes or aptamers, because these substances might bring about, similar to natural RNA, contact phase activation". Instant claim 1 recites "an amount, sufficient for promoting coagulation, of... peptide nucleic acids." The specification does not teach how a peptide nucleic acid can promote coagulation.

The specification does not offer guidance to resolve the known unpredictability in the art associated with appropriate *in vivo* delivery and treatment effects provided by the instantly claimed pharmaceutical preparations, and further does not offer guidance as to how a peptide-nucleic acid would predictably promote, rather than inhibit coagulation. The examiner is not asserting that the invention is drawn to an inhibitory effect, but rather that PNAs are known to have an inhibitory effect and that the specification has not taught an additional role of promoting coagulation. The references cited by the examiner were cited to demonstrate the known role and unpredictability of PNAs, which are a component of the instantly recited pharmaceutical preparation.

The specification as filed does not provide adequate guidance that would show how one skilled in the art would practice the claimed invention without undue experimentation. One of skill in the art would be forced to resort to undue trial and error experimentation.

Given the teachings of the specification as discussed above, one skilled in the art could not predict *a priori* whether introduction of peptide-nucleic acids *in vivo* by the broadly disclosed methodologies of the instantly claimed invention, would result in successful enhancement of coagulation *in vivo*. As explained in the office action mailed 11/7/2005, amendment to eliminate "a pharmaceutical preparation" from the preamble

and recitation of "in combination with pharmaceutically acceptable diluents" would obviate this rejection.

Response to Arguments--Claim Rejections - 35 USC § 102

Claim 1 stands rejected under 35 U.S.C. 102(b) as being anticipated by Shimkets et al. (WO 00/58473), as evidenced by Braasch et al. (Biochemistry, Vol. 41, No. 14, 2002, pages 4503-4510), for the reasons of record set forth in the office action mailed 11/7/2005.

Applicant argues that the amendment to claim 1 adding "an activator for plasma coagulation factor" to the pharmaceutical preparation of claim 1 should obviate the rejection because neither Shimkets et al. or Braash et al. teach an activator for plasma coagulation factor.

As explained in the 35 U.S.C. 103(a) rejection in the office action mailed 11/7/2005, the PNA or antisense oligonucleotide taught by Shimkets et al. is considered to meet the instant limitation of an activator for plasma coagulation factor because the instant specification discloses that any RNA is a potential activator for a plasma coagulation factor. This rejection is maintained because any PNA in a high enough concentration would lead to toxicity, followed by cellular death and coagulation, as evidenced by Braasch et al. Therefore, any PNA of the prior art formulated in a pharmaceutical composition would qualify as prior art when present in a high enough concentration to induce toxicity, since toxicity is correlated to a promotion of coagulation, as instantly recited.

Claim 1 stands rejected under 35 U.S.C. 102(b) as being anticipated by Moore et al. (US 6,248,724 B1), for the reasons of record set forth in the office action mailed 11/7/2005. This rejection is maintained for the same reasons as the Shimkets et al. rejection above. Applicant did not offer any additional arguments regarding this reference that have not been addressed above.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy H. Bowman whose telephone number is 571-272-0755.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For more information about the PAIR system, see http://pair-direct.uspto.gov.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Amy H. Bowman
Examiner
Art Unit 1635

JAMES SCHULTZ, PH.D.
PRIMARY EXAMINER